REMARKS/ARGUMENTS

Reconsideration of the application in view of the above amendments and following remarks is requested. Claims 1-3, 5-11, 14, and 26-34 are now in the case. Claims 1, 2, 5, 8, 26, 27, 28, and 29 have been amended. Claims 33 and 34 have been added. Claims 4, 12-13, and 15-25 are canceled. No new matter has been added.

Claim 29 has been amended for clarity and now recites that the additional polypeptide comprises an affinity tag. Support for this amendment is found throughout the specification as filed, such as at pages 9, 31, 41, and 50.

New claims 33 and 34 have been added to recite particular embodiments of Applicants' invention. Support for claims 33 and 34 is found within the specification as filed, such as at pages 7, 27, and 80-84.

The specification has been amended to remove embedded hyperlinks, correct the presentation of trademarks, and correct obvious typographical errors. No new matter has been added. These amendments are believed to overcome the Office's objections to the disclosure.

Claims 1, 5, 8, 26, and 27 were objected to because of the use of a comma following "(His)" and/or "(Met)." The commas have been deleted in the amended claims. It is believed that these amendments overcome this objection.

Claims 1-3, 5-11, 14, and 26-32 stand rejected under 35 U.S.C. § 101. The Office believes that the claimed invention is not supported by either a specific and substantial utility or a well-established utility.

This ground of rejection is respectfully traversed. Applicants believe that the Office has failed to establish a *prima facie* case of unpatentability. Moveover, in formulating the instant rejections, the Office has failed to comply with its own standards for examination as set forth in the Rules (including 37 C.F.R. § 1.104(d)), the MPEP, the Utility Examination Guidelines as published in the January 5, 2001 Federal Register, and the Revised Interim Utility Guidelines Training Materials.

To be considered useful under 35 U.S.C. § 101, an invention must have a specific, substantial and credible utility. It is well established that "when a properly claimed invention meets at least one stated objective, utility under §101 is clearly shown." *Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958 (Fed. Cir. 1983). That is, only a single utility for an invention need be disclosed in a patent application to satisfy the 35 U.S.C. § 101 utility requirement. Applicants respectfully submit that this burden has been met.

The polynucleotides recited in claims 1-3, 26-28, and 33-34 have a specific, substantial, and credible utility as probes. As disclosed by Applicants at pages 80-81 and 93-94 of the specification, the zlmda24 gene is located at the 7q21 region of

chromosome 7. Also as disclosed at page 80, an increase in copy number of chromosome 7 is the most common chromosomal abnormality observed in human malignant gliomas. One of ordinary skill in the art would readily comprehend that the claimed polynucleotides are useful for detecting duplications of chromosome 7, which are known to be associated with a specific disease. This use is specific (specific to the subject matter claimed), substantial (a "real world" use), and credible (believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided)[1]. In addition, other diseases and genetic abnormalities are known to be associated with duplication of chromosome 7 or aberrations of chromosome 7 at or about the 7q21 region (specification at pages 80-81), and the skilled practitioner would readily appreciate that the claimed polynucleotides would find additional utility in the diagnosis of such abnormalities.

The Office's own guidelines affirm the specific, substantial, and credible utility of the claimed polynucleotides. See, Revised Interim Utility Guidelines Training Materials at page 5:

> For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosomal marker" would not be considered to be *specific* in the absence of a disclosure of a specific DNA target. [Emphasis in original.]

Because Applicants have disclosed a specific DNA target (i.e., the 7q21 locus), a specific utility has been established. As discussed above, the specification further discloses the association of chromosome 7 duplications with glioma and the 7q21 locus with other genetic diseases. Thus, there is an art-recognized significance to the disclosed DNA target, and the disclosed utility is substantial and credible.

The Office has cited the disclosure of Ward as teaching "not all markers can be reliably used in primary diagnosis." Applicants respectfully submit that Ward is not germaine to the instant claims. Ward does not address the use of polynucleotide probes for detecting chromosomal abnormalities. Moreover, such a generalized statement is clearly refuted in the case of the claimed invention, wherein a specific polynucleotide sequence and a specific target are disclosed.

The Office relies on Critchfield to support the proposition that "it is apparent the skilled artisan could not immediately use the claimed invention in a manner that might benefit the public." Applicants respectfully submit that the Critchfield disclosure does not address the requirements of patentability. The views expressed by Critchfield are his own; they are not precedential in the realm of patent law. Moreover, Critchfield deals only in broad generalities (with the exception of BRCA testing), and

---

[1] The Office's Revised Interim Utility Guidelines Training Materials recognize the credibility of nucleic acids as probes. "However, nucleic acids could be used as probes, chromosome markers, or forensic or diagnostic markers." See, page 5.

does not address Applicants' claimed subject matter or disclosed utilities. As discussed herein, Applicants' have disclosed specific, substantial, and credible utilities that fulfill the criteria set forth in the Office's own Guidelines and Training Materials.

Polynucleotides as recited in claims 1-3, 26-28, and 33-34 would also be expected to find utility in histological applications. As disclosed in Applicant's specification at, for example, pages 14 and 90-93, zlmda24 is highly expressed in testis, and is not expressed in numerous other tissues and cell lines that were tested. Thus, polynucleotides encoding zlmda24 can be used directly as probes in *in situ* hybridization (as can fragments of such polynucleotides), or can be used to produce zlmda24 protein, which can be used to produce antibodies for use in immunohistochemistry. This latter utility also extends to the claimed DNA constructs (claims 8 and 29), expression vectors (claims 5, 6, 9, and 30), cultured cells (claims 7, 10, and 31), and methods of producing polypeptides (claims 11, 14, and 32). These are well-established, credible utilities as recognized by the Office's own Revised Interim Utility Guidelines Training Materials. See, pages 69-70:

> Let us assume for the moment that the specification also discloses that receptor A is present on the cell membranes of melanoma cells but not on the cell membranes of normal skin cells. . . . Based on the record, is there a "well established utility" for the claimed invention? The answer to this question would change to yes in each case. . . . Therefore, utility rejections under 35 U.S.C. § 101 rejection and a 35 U.S.C. § 112, first paragraph, should not be made against claims 1-3.

The use of probes and antibodies as controls in *in situ* hybridization and immunohistochemistry is disclosed by, for example, GeneDetect.com, "*In situ* hybridization - the issues," http://www.genedetect.com/insitu.htm, 2004 and Furuhashi et al., *Cancer Res.* 64:2725-2733, 2004 (copies enclosed).

The materials and methods for producing fusion proteins recited in claims 8-11 would be recognized by one of ordinary skill in the art as being useful for producing zlmda24 proteins. As discussed above, such proteins could be used, *inter alia*, to produce antibodies for use in immunohistochemistry. Fusion protein technology can be used, for example, to facilitate protein purification as disclosed in Applicants' specification at pages 9 and 50, to aid in protein secretion as disclosed at page 35, and to prolong clearance half-life (which may enhance immunogenicity) as disclosed at page 37.

The Office has also questioned the utility of complementary polynucleotide molecules (Office Action at p. 9). This aspect of the rejection is overcome in part and traversed in part. Claims 1, 2, and 26-28 have been amended to cancel the subject matter in question. New claim 34 recites an isolated polynucleotide comprising at least 14 contiguous nucleotides of SEQ ID NO:1 or the complement of

SEQ ID NO:1, wherein said polynucleotide hybridizes to the 7q21 region of human chromosome 7 under hybridization wash conditions of 0.1x SSC to 0.2x SSC, 0.1% SDS at 55°C-65°C. The claimed polynucleotide is useful as a probe, such as a probe for chromosomal abnormalities associated with malignant gliomas, as discussed above.

The utilities shown by Applicants for the claimed polynucleotides, DNA constructs, expression vectors, cultured cells, and methods of producing polypeptides are specific, substantial, and credible. The "specific" and "substantial" requirements are intended to exclude "throw-away" utilities, such as use of a complex invention as landfill. In contrast, Applicant has shown usefulness for particular, practical purposes. As to credibility, Applicant's assertions are backed by laboratory data as shown in the specification, for example in Examples 2 and 3, and by the disclosures of GeneDetect.com and Furuhashi et al. "[I]f applicant makes one credible assertion of utility, utility for the claimed invention as a whole is established." MPEP 2107.01. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 101 are respectfully requested.

Claims 1-3, 5-11, 14, and 26-32 stand rejected under 35 U.S.C. § 112, first paragraph. The Office believes that "since the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility for the reasons set forth [] above, one skilled in the art clearly would not know how to use the claimed invention."

This ground of rejection is respectfully traversed. The underlying § 101 utility rejection has been addressed in detail above. Applicants have established that the claimed invention is supported by at least one specific, substantial, and credible utility, and/or a well-established utility. Thus, the rejection under § 112, first paragraph, is also overcome. In addition, detailed disclosure of how to use the invention is provided by Applicants' specification. See, for example, pages 79-84 and 93-94. Reconsideration and withdrawal of this rejection are requested.

Claims 1-3, 5-11, 14, and 26-32 stand rejected under 35 U.S.C. § 112, first paragraph. The Office believes that the claims fail to comply with the written description requirement. The Office further believes that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is traversed in part and overcome in part. To the extent that the rejection is based on the recitation of complementary polynucleotides, claims 1-3, 5-11, 14, and 26-32 have been amended to remove such recitation. New claim 34 recites an isolated polynucleotide comprising at least 14 contiguous nucleotides of SEQ ID

NO:1 or the complement of SEQ ID NO:1, wherein said polynucleotide hybridizes to the 7q21 region of human chromosome 7 under hybridization wash conditions of 0.1x SSC to 0.2x SSC, 0.1% SDS at 55°C-65°C. Such a polynucleotide is clearly described within the specification as filed, which includes a full disclosure of SEQ ID NO:1, which further conveys to one of ordinary skill in the art the complement of SEQ ID NO:1. The remaining claims, as amended, recite a polynucleotide that encodes the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 32 to amino acid number 253 or from amino acid number 1 to amino acid number 253.

The Office has asserted that Applicants have failed to disclose "particularly identifying characteristics of SEQ ID NO: 1 or SEQ ID NO: 5, or the protein encoded thereby, that are shared by at least a substantial number of the other members of the claimed genus." Applicants strongly disagree with the Office's characterization of the disclosure. Claims 1-3, 5-11, 14, and 26-33 recite specific regions of SEQ ID NO:1, NO:2, and NO:5, which regions include or encode at least amino acid residues 32-253. The claimed members share these "particularly identifying characteristics." Claim 34 recites an isolated polynucleotide comprising at least 14 contiguous nucleotides of SEQ ID NO:1 or the complement of SEQ ID NO:1, wherein said polynucleotide hybridizes to the 7q21 region of human chromosome 7 under hybridization wash conditions of 0.1x SSC to 0.2x SSC, 0.1% SDS at 55°C-65°C. Thus, the invention of claim 34 is clearly and extensively characterized in the claim.

The Office has further asserted that "claims 11, 14, and 32 are directed to a method for producing any member of a genus of fusion proteins or polypeptides" and that "the specification does not describe the other fusion proteins or polypeptides." Applicants wish to direct the Office's attention to the specification, such as at pages 9, 35, 37, 41, 45, and 50-51, wherein a variety of fusion proteins are disclosed. Moreover, fusion protein technology is well-established in the art. Peptide tags for use in protein purification are commercially available as disclosed in Applicants' specification at page 9. Immunoglobulin fusion proteins are disclosed in U.S. Patents Nos. 5,155,027 and 5,567,584 (specification at page 41). Persons of ordinary skill in the art routinely produce these and other types of fusion proteins for a variety of purposes. There is no requirement for Applicants to disclose the details of such well established technologies. "A patent need not teach, and preferably omits, what is well known in the art." (*Spectra Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 3 USPQ2d 1737 (Fed. Cir. 1987), *cert. denied*, 484 U.S. 954 (1987).)

Reconsideration and withdrawal of this rejection are requested.

Claims 1, 2, 26, and 28 stand rejected under 35 U.S.C. § 112, second paragraph. The Office believes that the claims are indefinite for failing to particularly

point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Office believes that it cannot be determined if "(c) a polynucleotide sequence complementary to (a) or (b)" is, or is not, a third member of the Markush groups recited in the claims.

This rejection is believed to be overcome by the amendment of claims 1, 2, and 26-28. The amended claims do not recite "a polynucleotide sequence complementary to (a) or (b)." Reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph are requested.

Claims 1, 2, and 26-28 stand rejected under 35 U.S.C. § 102(b). The Office believes that these claims are anticipated by Boehringer Mannheim Biochemicals, 1994 Catalog. Boehringer Mannheim is cited as teaching a collection of random primers, allegedly a collection that "comprises primers having a polynucleotide sequence that is completely complementary to any and every 6 nucleotide fragment of a polynucleotide encoding a polypeptide comprising the amino acid sequence, or a specified portion thereof, of SEQ ID NO:2."

This rejection is respectfully traversed. The rejected claims recite "isolated" polynucleotides, which are defined at page 11 of Applicants' specification as "free of other extraneous or unwanted coding sequences, and [] in a form suitable for use within genetically engineered protein production systems." The Office has not explained how a mixture of random hexa-nucleotides falls within this definition. Furthermore, even an isolated and purified hexa-nucleotide does not anticipate or make obvious the subject matter of amended claims 1, 2, and 26-28. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(b) are requested.

The claimed invention is believed to be patentable over all art of record.

Applicants believe that each rejection has been addressed and overcome. Reconsideration of the application and its allowance are requested. If for any reason the Examiner feels that a telephone conference would expedite prosecution of the application, the Examiner is invited to telephone the undersigned at (206) 442-6673.

Respectfully Submitted,

Gary E. Parker
Registration No. 31,648

Enclosures:

Amendment Fee Transmittal (in duplicate)
Petition and Fee for Extension of Time (in duplicate)
Letter
2 References
Postcard

Gary E. Parker
ZymoGenetics, Inc.
1201 Eastlake Avenue East
Seattle, WA 98102
Tel. (206)442-6673
Fax (206)442-6678